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NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
5	06/07/1999	JENNIE BIH-JIEN SHEN	BB-1137	4005

7590 03/21/2002

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EXAMINER	
EINSMANN, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	18

DATE MAILED: 03/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/326,285	SHEN, JENNIE BIH-JIEN
Examiner	**Art Unit**
Juliet Einsmann	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 08 January 2002.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-150,169,170 and 172-176 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-150,169,170 and 172-176 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 11/5/01, a copy of which was faxed to the office on 1/8/02, paper number 14. Claim 175 has been amended. Claims 1-150, 169, 170, and 172-176 are pending. Elected claims 172-176 are examined herein. Applicant's amendments and arguments have been thoroughly reviewed, but are not fully persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Election/Restrictions

2. The elected claims contain subject matter that is drawn to a non-elected invention (i.e. SEQ ID NO: 11). A complete reply to the final rejection must include cancellation of non-elected subject matter from the claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Information Disclosure Statement

3. The references mailed with the instant response have been received. These reference have been considered and initialed on the appropriate 1449's.

Claim Rejections - 35 USC § 112

Second Paragraph

4. Claims 172-176 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 172-176 are indefinite over the recitation of the phrase "carcass quality improving amount" because it is not clear exactly what amount of an animal feed would constitute a carcass quality improving amount. The specification provides no guidance in the determination of such an amount, and therefore the metes and bounds of this claim are unclear.

Claims 172-176 are indefinite over the recitation of "reverse complement" because it is not clear what this terminology means. For example, given the sequence 5'-CAT-3', the complement is 3'-GTA-5' or 5'-ATG-3'. It the reverse complement then 5'-GTA-3'?

Claims 172-176 are indefinite over the recitation of "or a functionally equivalent subfragment thereof." It is not clear, for example, if this phrase is referring to the nucleic acid in the chimeric gene or to SEQ ID NO: 9.

Claims 172-174, sections (ii) and (iv), and claim 175 (b) are indefinite over the phrase "the isolated nucleic acid fragment comprising a full length or partial corn" because this phrase is unclear. That is, it is not clear which nucleic acid is being referred to when the claim recites "the isolated..."

Claims 172-174, sections (ii) and (iv), claim 175 (b), and claim 176 are indefinite over the language "corn oleosin promoter hybridizes to the" because this language is unclear.

First Paragraph

5. Claims 172-176 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 172-176 are drawn to methods of improving animal carcass quality by feeding an animal a "carcass quality improving" amount of animal feed derived from transgenic plants which comprise chimeric genes as listed in the claims. These claims are broadly drawn in that they encompass methods for improving the carcass quality of any animal, and they do not specifically indicate the amount of feed necessary to effect the goal of improving carcass quality. Further, as discussed above, neither the claims nor the specification offer guidance as to how to measure carcass quality or what aspect of carcass quality would be improved by the consumption of the animal feed derived from the plants described in the claims.

The prior art provides no guidance as to the expected effects of feeding plants with altered lipid content on carcass quality of animals. Furthermore, experiments in the prior art indicate that the effects changes in feeding regimes will have on animal carcass quality are highly unpredictable. For example, Machev *et al.* (Zhivotnov"dni Nauki, (1996) Vol. 33, No. 3, p. 23-26) found that completely replacing maize with barley in animal feed had no significant effect on the slaughter and commercial value of pigs (ABSTRACT, p. 26). Certainly the difference in the nutritional content of barley versus maize in animal feed would be expected to be larger than the overall difference between wild type corn and the corn used in the present invention. Cooke *et al.* (Anim. Prod. (1971) Volume date 1970, 14(P1. 2) 219-28, ABSTRACT only) failed to demonstrate any significant interaction between dietary energy and protein in terms of carcass tissue proportions. These references are cited merely to demonstrate that it is highly unpredictable as to how feeding regimes will effect the carcass quality of animals.

The specification teaches plants with two different alterations in fatty acid content, some with increased saturated acid content, and some with oleic acid content. The specification provides no guidance as to how either type of plant can be used to improve carcass quality. The specification provides no guidance as to which animals will be expected to have their carcasses improved, during what part of the feeding regime the animals should be fed the plants comprising the chimeric genes, how much feed would be "a carcass quality improving amount" or how the ordinary practitioner should measure the improvement in carcass quality. The determination of such factors would require extensive experimentation with a wide variety of animals, and such experimentation would in itself be inventive.

Due to the broad nature of the claims, the lack of guidance in the specification or in the prior art, the high level of unpredictability with regard to the effects of feeding regimes on animal carcass quality, the lack of working examples, and the high level of experimentation necessary to determine the methodology necessary to practice the claimed invention, it is concluded that undue experimentation would be required to practice the claimed invention.

Furthermore, with regard to the plants that are described to be used as animal feed, the does not reasonably provide enablement for the claimed plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the plants commensurate in scope with these claims.

The specification teaches corn plants which have high stearic acid content (compared to wild type) in corn grains after transformation with chimeric constructs that contain either the anti-sense (pBN262) or sense (pBN264 or pBN427) strands of a truncated corn delta-9 desaturase (a truncated version of the full length SEQ ID NO: 9). The specification also teaches

corn plants with high oleic acid content (compared to wild type) in corn grains after transformation with chimeric constructs that comprise a near full length fad2-1 coding region with the ATG out of frame (pBN257 (SEQ ID NO: 58) or construct pBN428). The specification discusses possible mechanisms for producing plants with high stearic acid content and high oleic acid content, but does not exemplify such plants.

The specification does not teach any general mechanism by which the introduced nucleic acids are effecting the fatty acid content of the plants. The specification does not teach a plants with a broad range in changes in fatty acid composition, only plants with high stearic acid content or high oleic acid content. The specification also does not teach plants which comprise both of the desaturases in which altered lipid content is observed.

It is highly unpredictable which nucleic acid sequences would result in the alteration of the lipid profile of plants. That is, although transformation of the plants with the corn deasturases described in the claims may be possible, the effect of using, for example, a full length sense copy of corn delta-9 stearoyl ACP desaturase on a plant is highly unpredictable. The specification teaches plants in which sense and anti-sense nucleic acids encoding corn delta-9 stearoyl ACP desaturase are introduced into plants, and in both instances the resulting plant displayed high saturate fatty acid composition. The mechanism by which this occurs is unclear, and therefore, it is not possible to predict the effect that adding other nucleic acids to the plants would have on the plant. Inhibition of the functioning of the native enzyme by an introduced nucleic acid is expected to be sequence dependent, and the specification provides no guidance as to how the instant nucleic acids can be altered so as to produce plants with similar alterations in fatty acid composition. The claims are broadly drawn to include the use of plants transformed

with any portion of nucleic acids encoding a desaturase with 80% identity to the disclosed desaturase or with any functional fragment thereof. However, the specification provides no guidance as to how the nucleic acids of the examples can be modified and still have the same effect on a plant upon transformation of the plant with the nucleic acid. The experimentation necessary to determine other plants would require the production of many plants using many different nucleic acids, both sequence variants of the disclosed nucleic acids and fragments of the disclosed nucleic acids, assaying the produced plants for lipid content and analyzing the results for an association between different nucleic acids an changes in lipid content.

Due to the lack of guidance in the specification, the high level of experimentation that would be required to make other plants with altered lipid content, and the high level of unpredictability with regard to which nucleic acids would be useful for producing such plants, undue experimentation would be required to produce animal feed from plants as broadly claimed.

6. Claims 172-176 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claims are drawn to a method which improving animal carcass quality which comprise feeding the animal feed derived from transgenic plants comprising chimeric molecules which comprise nucleic acids encoding a corn delta-9 stearoyl ACP desaturase which has an amino acid sequence with 80% identity to SEQ ID NO: 9, nucleic acids encoding a corn delta-12 desaturase wherein the nucleic acid has 80% sequence identity to SEQ ID NO: 1, or functional

fragments of either of these two nucleic acids. Further, the claims include plants comprising promoters with 80% identity to SEQ ID NO: 19 or 38-49 or which hybridize to SEQ ID NO: 19 and 38-49 under moderate stringency conditions. This large genus is represented in the specification by only SEQ ID NO: 9, SEQ ID NO: 1, or SEQ ID NO: 19 and 38-49, as appropriate. Further, the response of the plants produced largely depends on the functionality of the sequence introduced. Thus, applicant has express possession of only single species in a genus which comprises hundreds of millions of different possibilities.

With regard to the written description, all of these claims encompass nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claims 172-176 include modifications by permitted by the % identity language or the "functionally equivalent subfragment" language for which no written description is provided in the specification. Especially with regard to the functionally equivalent subfragment language, the mechanism by which the introduced nucleic acids act in plants is unknown, and therefore the "function" of the nucleic acids in the plants is unknown.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the SEQ ID NO: 1 is described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention

being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of any plants containing chimeric genes modified by addition, insertion, deletion, substitution or inversion with the disclosed SEQ ID Nos but retaining correlative function in the claimed product.

Response to Remarks

Applicant's remarks concerning each of the reiterated rejections have been considered but are not persuasive.

112 2nd paragraph

Applicant argues that "carcass quality improving amount" is quite clear to one of ordinary skill in the art. However, the examiner does not agree. While the term "carcass quality" may be well defined in the prior art, the "carcass quality improving amount" described herein is not defined in either the prior art or the specification. The specification lacks any definition as to how much of the instant animal feed derived from the processing of corn grain constitutes a carcass quality improving amount. The skilled practitioner has no way of knowing from the disclosure in the specification (or the prior art) how much animal feed derived from the processing of corn grain from the disclosed transgenic plants would be within the metes and bounds of these claims. The purpose of the claim is to clearly define the boundaries of the invention, and in this case, the claim provides no boundary for the amount of feed that is being fed to animals in the only active process step of the claim.

Applicant argues that the "reverse complement" in the claims is what the Examiner refers to as the complement on page 4 of the Office Action. However, this argument is not persuasive

to overcome the 112 2nd rejection because this definition of "reverse complement" is contrary to the art accepted meaning of a reverse complement, which implies the reverse sequence of the complement of a nucleic acid sequence. The specification does not describe the "reverse complement" with respect to antisense RNA, but instead describes antisense RNA as "a transcript that is complementary to all or part of a target primary transcript (page 16 of the specification)."

Applicant asserted out that the term "functionally equivalent fragment" is defining the corn delta-9 stearoyl ACP desaturase. If the "functionally equivalent fragment" language is meant to refer to the desaturase (i.e. the enzyme which has an amino acid sequence) then the language which follows that refers to "the reverse complement of either the fragment or subfragment" does not make sense because the subfragment would be an amino acid sequence and would not have a reverse complement.

Applicant's comment about "the isolated nucleic acid fragment comprising a corn oleosin promoter" does not clarify the claims. For example, claim 172, in part (ii) currently recites a "chimeric gene comprising (a)...., and (b) an isolated nucleic acid fragment comprising a corn oleosin promoter wherein said promoter can be full length or partial and said promoter: (1) comprises.... OR (2) the isolated nucleic acid..." Thus, there is no transition to introduce "the isolated nucleic acid" of part (b)(2), which is presented as an alternative of (b)(1) because the transitional phrase "comprising" is part of (b)(1). Thus, the claims remain indefinite. Essentially, part (ii)(b)(2) reads "an isolated nucleic acid fragment comprising a corn oleosin promoter wherein said promoter can be full length or partial and **said promoter the isolated** nucleic acid comprising a full length or **partial corn oleosin promoter hybridizes** to the

nucleotide sequence..." The language appears to be missing key transitional phraseology and thus renders the claims confusing and indefinite.

112 1st paragraph

Applicant begins the remarks by pointing out the many factors involved in evaluating carcass quality, citing a number of different references to define "carcass quality" and methods for measuring carcass quality. However, these definitions do not remove the fact that the specification has provided no guidance as to which aspect of carcass quality will be improved by the practice of the instant method, nor does the specification provide sufficient guidance as to how to practice the single critical step of feeding the animals. The specification provides no guidance as to what amount of feed derived from the transgenic corn of interest is necessary to effect the improvement of any aspect of carcass quality. Applicant argues that the references cited in the office action are irrelevant to the instant inquiry because they concern replacing maize with barley as opposed to replacing one type of corn with another type of corn. The references were included to demonstrate that attempts to alter carcass quality by changing the type of plant from which animal feed is derived is highly unpredictable. The references provide evidence that when food with nutritional profiles that are certainly less similar than the two types of corn in the instant inquiry, there is no apparent change in the carcass quality of the subject animals. The instant specification does not provide any evidence that the transgenic corn of the instant invention would result in an increase in the carcass quality of animals who eat the corn.

Applicant draws the Examiner's attention to the fact that the specification describes (1) transgenic plants with high saturate fatty acid composition in grain (2) transgenic corn with a

high oleic acid content in the grain and (3) transgenic corn with high levels of saturated and oleic acid in kernels, thus concluding that the specification and examples show one of ordinary skill in the art how to practice the claimed invention. This statement is problematic on a number of grounds. First, it is noted that the specification only actually demonstrates the production of plants in the category of (1) and (2). The third type of plants were never made, the examples in the specification are only prophetic. Even in light of the making of these plants, however, the specification does not provide any guidance related to the instantly claimed invention, which is drawn to a method for improving animal carcass quality, as has been discussed above.

With regard to the scope of enablement for the production of transgenic plants, Applicant's arguments do not adequately address the discussion of the Wands factors provided in the enablement rejection. The conclusion that undue experimentation would have been necessary to make transgenic plants commensurate in scope with those used in the instant method claims is base was made because of the lack of guidance in the specification, the high level of experimentation that would be required to make other plants with altered lipid content, and the high level of unpredictability with regard to which nucleic acids would be useful for producing such plants, undue experimentation would be required to produce animal feed from plants as broadly claimed. Applicant has demonstrated for only a small portion of the broad range in the claims the making of the transgenic plants used in the claimed invention. The fact that both sense and anti-sense constructs to the same gene yield the same effect (high saturate fat composition) in the transgenic plants underscores the assertion that the state of the art with regard to the production of transgenic plants displaying this particular phenotype is highly unpredictable. While it is not necessary that applicant understand the mechanism of the action in

these transgenic plants, such a relationship would be helpful to help overcome the concerns regarding the unpredictabilty of the claimed invention. The specification provides only two working examples which use a particular nucleic acid sequence to effect the goal of increasing saturate fatty acid composition in transgenic corn. The specification provides no guidance as to how those sequences could be modified yet still yield plants with the same phenotype, nor does the specification provide any guidance as to how a plant with high saturate fatty acid composition could be used to improve the carcass quality of animals. In light of each of these factors, it was concluded by the examiner that undue experimentation would be necessary to make transgenic plants commensurate in scope with those described in the elected claims, and further to practice the methods of the claimed invention.

Further pending is a 112 1st paragraph rejection directed to the lack of written description of the claimed invention. Applicant points out that the specification defines "functionally equivalent subfragment" and discusses percent identity language. However, these definitions do not overcome the fact that the claims are not supported by adequate written description. The claims provide a structure for the nucleic acids to be used in the transformation, but the claims do not provide an adequate functional language relating to that structure. Thus the claims embrace the use of nucleic acids that are not properly described with a structure-function relationship. Notwithstanding, even if the claims did include a proper structure function relationship to describe the nucleic acids, it is not clear that this language would be sufficient to overcome the rejections directed towards lack of enablement of the claimed invention.

Conclusion

7. No claims are allowed.

8. Nucleic acids consisting of SEQ ID NO: 19 and 38-49 are free of the prior art.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Einsmann
Examiner
Art Unit 1655

March 14, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600